REMARKS

Claims 11, 45, 47-52, 57, 58 and 60 are pending in this application. Claim 47 has been amended. No new matter has been added.

Based upon the arguments made herein, the present application should be in condition for allowance. If the Office does not agree, Applicants respectfully request that the Office call Applicants' attorney, Laurie Butler Lawrence, at 617-395-7088 to discuss the outstanding issues.

Claim Objections (Informalities)

At page 2 of the Office Action, claim 47 was objected for depending from a cancelled claim. Claim 47 has been amended to depend from claim 11, thereby obviating this objection.

Rejection Under 35 U.S.C. §112, first paragraph

Claims 11, 45, 47-52, 57, 58 and 60 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Office, "the phrase 'amino terminal domain of a mammalian CC-chemokine receptor 2' as recited in independent claim 11 is not supported by the original disclosure or claim as filed." The Office alleges that " The specification only discloses antibody that binds to CCR-2 or a portion of CCR-2 … the instant claims now recite any antibody that binds to the 'amino terminal domain of mammalian CC-chemokine receptor 2' which were not clearly disclosed in the specification."

Applicants respectfully traverse this rejection. The application as originally filed explicitly describes antibodies that bind to the amino-terminal domain of a mammalian CCR-2. Page 12, lines 10-12, of the application states that "the invention pertains to an antibody or functional portion thereof which binds to the amino-terminal domain or a portion thereof of mammalian CC-chemokine receptor 2." Furthermore, the application describes several antibodies that bind to the amino-terminal portion of mammalian CCR2. For example, page 12, lines 3-4, of the application states that "the binding site of mAbs 1D9 and 8G2 has been mapped to the amino-terminal domain of human CC-chemokine receptor 2." In addition, page 9, lines 1-2, describe an antibody 5A11 "generated using a peptide consisting of the first 32 amino acids of the CCR2 amino-terminus as an immunogen." Thus, the application as originally filed clearly

describes anti-CCR2 antibodies which bind the amino terminal domain of mammalian CCR2, and therefore, claims directed to antibodies and antigen binding fragments thereof that bind this portion of CCR2 are not new matter.

Applicants respectfully request that the Office withdraw this rejection.

Rejection Under 35 U.S.C. §103 (Obviousness)

At pages 4 to 6 of the Office Action, claims 11, 44, 45, 47, 48, 57, 58 and 60 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Lind et al. (U.S. Patent No. 6,084,075) in view of Hardiman et al. (U.S. Patent No. 7,115,379). In addition, at pages 6 and 7 of the Office Action, claims 49-52 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Lind et al. (*supra*) and Hardiman et al. (*supra*) as applied above, and further in view of Lam et al. (U.S. Patent No. 6,171,586).

According to the Office,

> in contrast to applicant's reliance on the working examples of Lind et al regarding the agonistic antibody MCPR-02, it is noted that the teachings of Lind et al. are not merely limited to these working examples. Lind et al. identified that the N-terminal domain of the CCR2 and teach not only how to make an antibody that binds to the N-terminal domain but also how to screening for the properties of said antibody.
>
> Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to make an antagonistic anti-CCR2 antibody that binds the N-terminal domain.

Applicants respectfully traverse these rejections. Contrary to the allegations made in the Office Action, Applicants' position regarding the teaching of Lind et al. are not limited to just the examples in that reference. The Office provides an over generalized statement that Lind et al. teach antibodies that bind the N-terminal domain. However, in reality, Lind et al. teach that antibodies that bind to the N-terminal domain of CCR2 are agonist of CCR2. This point is highlighted throughout the Lind et al. reference. For example, column 4, lines 42-62 of Lind et al. state that "we have generated mAb specific for the CCR2 chemokine receptor by immunizing mice with synthetic peptides corresponding to several extracellular receptor domains" and "using these mAb, we **define CCR2 regions critical for ligand binding** and **for eliciting a response**

through this receptor. Based upon the ability of these mAb to trigger chemokine receptors or to block chemokine responses, we have outlined a model that takes into account our present knowledge of chemokine responses." In the very next paragraph Lind et al. conclude that "in contrast to IL-8 neutralizing antibodies which are directed to the NH2 terminal region, our mAb with antagonistic activity (MCPR-4 and MCPR-05) map to the third extracellular loop of the CCR2 receptor". In the very same paragraph, Lind et al. discuss the "surprising fact that amino terminal specific mAb, for example MCPR-02, can **mimic** the chemokine response" and conclude that "**[t]his allows us to consider this region critical in agonist activation of the CCR2 receptor.**" (**emphasis added**). Lind et al. also state "we therefore conclude that chemokine receptors are organized into two distinct functional domains, corresponding to the NH2 terminal and third extracellular loop region." There is no ambiguity to the teaching of Lind et al. Lind et al. clearly teach that antibodies that bind to the N-terminal domain of CCR2 act as agonist.

This point is further emphasized by the examples provided in the Lind et al. reference. For example, at column 12, lines 28-34, Lind et al. state that

> Three mAb (MCPR-04, -05 and -06) act as antagonists of the receptor, as they block the MCP-1-induced calcium flux in Mono-Mac-1 cells (Fig. 2). The **antibodies with antagonistic activity recognize the third extracellular** loop of the receptor (aa 273-292) while **the agonistic antibody recognizes the amino terminal region** (aa 24-38). (**emphasis added**)

Based upon the teachings of Lind et al., one of ordinary skill in the art wanting to make an antibody that functions as an antagonist of CCR2 would not have raised an antibody to the N-terminal domain of CCR2. A skilled artisan reading Lind et al. would not have predicted that an antibody raised to the N-terminal domain of CCR2 would inhibit the binding of a chemokine to the receptor, and inhibit one or more functions associated with the chemokine receptor, as required by the claims.

Neither Hardiman et al. nor Lam et al. cure the aforementioned deficiencies of Lind et al. Neither of these references teach or suggest an antibody that binds CCR2, much less an antibody that binds the N-terminal domain of CCR2 and functions as an antagonist.

Therefore, since none of the cited references, alone or in combination, teach or suggest antibodies that possess the structural and functional characteristics required by the claims or kits containing such antibodies, the references do not render the claims obvious. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

For the reasons set forth above, Applicants submit that all grounds for objection and rejection have been overcome and that all of the pending claims are now in condition for allowance, which action is earnestly requested. Applicants do not accede to any positions of the Examiner not specifically addressed above.

A three month extension fee is being paid concurrently by deposit account authorization. Please charge any deficiency to Deposit Account No. 50/2762, referencing attorney docket number M2051-701422.

Respectfully submitted,

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